

**Amendments to the Specification:**

- Please replace the paragraph on page 7, starting at line 20 with the following text:

Figure 1 shows amino acid sequence of the B4ECv3 protein (predicted sequence of the precursor including uncleaved Eph B4 leader peptide is shown), SEQ ID NO: 386.

- Please replace the paragraph on page 7, starting at line 22 with the following text:

Figure 2 shows amino acid sequence of the B4ECv3NT protein (predicted sequence of the precursor including uncleaved Eph B4 leader peptide is shown), SEQ ID NO: 387.

- Please replace the paragraph on page 7, starting at line 24 with the following text:

Figure 3 shows amino acid sequence of the B2EC protein (predicted sequence of the precursor including uncleaved Ephrin B2 leader peptide is shown), SEQ ID NO: 388.

- Please replace the paragraph on page 7, starting at line 26 with the following text:

Figure 4 shows amino acid sequence of the B4ECv3-FC protein (predicted sequence of the precursor including uncleaved Eph B4 leader peptide is shown), SEQ ID NO: 389.

- Please replace the paragraph on page 7, starting at line 28 with the following text:

Figure 5 shows amino acid sequence of the B2EC-FC protein (predicted sequence of the precursor including uncleaved Ephrin B2 leader peptide is shown), SEQ ID NO: 390.

- Please replace the paragraph on page 18, starting at line 21 with the following text:

Figure 61 shows a genomic nucleotide sequence of human EphB4, SEQ ID NO: 391.

- Please replace the paragraph on page 18, starting at line 22 with the following text:

Figure 62 shows a cDNA nucleotide sequence of human EphB4, SEQ ID NO: 392.

- Please replace the paragraph on page 18, starting at line 23 with the following text:

Figure 63 shows a genomic nucleotide sequence of human Ephrin B2, SEQ ID NO: 393.

- Please replace the paragraph on page 18, starting at line 24 with the following text:

Figure 64 shows a cDNA nucleotide sequence of human Ephrin B2, SEQ ID NO: 394.

- Please replace the paragraph on page 18, starting at line 25 with the following text:

Figure 65 shows an amino acid sequence of human EphB4, SEQ ID NO: 395.

- Please replace the paragraph on page 18, starting at line 26 with the following text:

Figure 66 shows an amino acid sequence of human Ephrin B2, SEQ ID NO: 396.

- Please replace the paragraph bridging pages 49 and 50 with the following text:

Plasmids vectors for expressing recombinant soluble derivatives of Ephrin B2 and EphB4 were based on pEF6/V5-His-TOPO vector (Invitrogen), pIG (Novagen) or pRK5.

pEF6/V5-His-TOPO contains human elongation factor 1 $\alpha$  enhancer/promoter and blasticidin resistance marker. pIG vector is designed for high-level expression of protein fusions with Fc portion of human IgG1 under CMV promoter control and pRK5 is a general purpose CMV promoter-containing mammalian expression vector. To generate plasmid construct pEF6-B4EC-NT, cDNA fragment of human EphB4 was amplified by PCR using oligo primers 5'-GGATCCGCC ATGGAGCTC CGGGTGCTGCT-3' (SEQ ID NO: 1) and 5'-TGGATCCCT GCTCCCGC CAGCCCTCG CTCTCATCCA-3' (SEQ ID NO: 2), and TOPO-cloned into pEF6/V5-His-TOPO vector. pEF6-hB4ECv3 was derived from pEF6-B4ECNT by digesting the plasmid DNA with EcoRV and BstBI, filling-in the ends with Klenow enzyme and religating the vector. Recombinant EphB4 derivative encoded by pEF6-B4EC-NT does not contain epitope- or purification tags, while the similar B4ECv3 protein encoded by pEF6-hB4ECv3 contains V5 epitope tag and 6xHis tag on its C-terminus to facilitate purification from conditioned media. Plasmid construct pEF6-hB2EC was created by PCR amplification of Ephrin B2 cDNA using oligo primers 5'- TGGATCCAC CATGGCTGT GAGAAGGGAC-3' (SEQ ID NO: 3) plus 5'- ATTAATGGTGGTGGT GAT GATGACTAC CCACTTCGG AACCGAGGATGTTGTTC-3' (SEQ ID NO: 4) and TOPO-cloning into pEF6/V5-His-TOPO vector. Plasmid construct pIG-hB2EC-FC was created by PCR amplification of Ephrin B2 cDNA with oligo primers 5'-TAAAGCTTCCGCCATGG CTGTGAGAAGGGAC-3' (SEQ ID NO: 5) and 5'-TAGGATCCACTTCGGA ACCGAGGATGTTGTT CCC-3' (SEQ ID NO: 6), followed by TOPO-cloning and sequencing the resulting PCR fragment with consecutive subcloning in pIG hIgG1 Fc fusion expression vector cut with Bam HI and Hind III. Similarly, pIG-hB2EC and pIG-hB4ECv3 were generated by PCR amplifying portions of EphB4 ECD cDNA using oligo primers 5'-ATAAGCTTCC GCCATGGAGC TCCGGGTGCTG-3' (SEQ ID NO: 7) plus 5'-TTGGATCCTGCTCCCG CCAGCCCTCGC TCTCATC-3' (SEQ ID NO: 8) with consecutive subcloning into pIG hIgG1 Fc fusion expression vector cut with Bam HI and Hind III. Predicted sequences of the proteins encoded by the vectors described above are shown in Figures 1-5.

➤ Please replace the paragraph bridging pages 58 and 59 with the following text:

To construct expression vectors for producing soluble, 6xHis-tagged EphB4-ECD variants, cloned full-length human EphB4 cDNA was amplified by PCR using the following oligo primers: TACTAGTCCGCCATGGAGCTCCGGGTGCTGCT (SEQ ID NO: 9) (common EphB4 N-terminal primer) and GCGGCCGCTTAATGGTGGTGA TGATGAGCCGA AGGAGGGGTGGTGCA (SEQ ID NO: 10) (B4-GC), AGCGGCCGCTTAATGGTGGTGA

TGAT GATGGACATTGA CAGGCTCAAATGGGA (SEQ ID NO: 11) (B4-GCF1) or TGCGGCCGCTTAATG GTGATGGTGATGAT GCTGCTCCCGCCAGCCCTCGCTCTCAT (SEQ ID NO: 12) (B4-GCF2). The resulting PCR fragments were TA-cloned into mammalian expression vector pEF6/V5-His-TOPO (Invitrogen) under EF-1 $\alpha$  promoter control. The expressed recombinant proteins encode the following fragments of the mature extracellular part of human EphB4: amino acid positions 1-522 (GCF2), 1-412 (GCF1) and 1-312 (GC). To generate the B4-CF2 deletion ( $\delta$  amino acids 13-183) PCR fragment for pEF6 cloning, EphB4 cDNA was amplified by two-step overlap PCR using oligo primers TACTAGTCCGCCATGGA GCTCCGGGTGCTGCT (SEQ ID NO: 13), CAGCTGAGTTTCCAATTTTGTGTTC (SEQ ID NO: 14), GAACACAAAATTGGAACTCAGCTGACTGTGAACCTGAC (SEQ ID NO: 15) and GCGGCCGCCCTG CTCCCGCCAGCCCTCGCT (SEQ ID NO: 16).

- Please replace the paragraph on page 59 starting at line 11 with the following text:

Vector for producing secreted human EphrinB2-alkaline phosphatase (B2-AP) reagent was constructed by PCR amplification of human Ephrin B2 cDNA using primers TAAAGCTTCCGCCATGGCTGTGAGAAGGGAC (SEQ ID NO: 17) and TAGGATCCTTCG GAACCGAGGATGTTGTTCCC (SEQ ID NO: 18) and cloning the resulting fragment, digested with Hind III and Bam HI, into Hind III-Bgl II digested pAPTag2 vector (GenHunter, Inc.). In each case, inserts in expression vectors were verified by complete sequencing.

- Please replace the paragraph on page 68 starting at line 15 with the following text:

EphB4 specific antisense phosphorothioate-modified oligodeoxynucleotide (ODN) and sense ODN were synthesized and purified by Qiagen (Alameda CA). The sequences are: Sense, 5'-TCC-TGC-AAG-GAG-ACC-TTC-AC-3' (SEQ ID NO: 19); AS1: 5'-GTG-CAG-GGA-TAG-CAG-GGC-CAT-3' (SEQ ID NO: 20); AS10: 5'-ATG-GAG-GCC-TCG-CTC-AGA-AA-3' (SEQ ID NO: 21). siRNAs were synthesized at the USC/Norris Comprehensive Cancer Center Microchemical Core laboratory. Sequences of EphB4 siRNAs are siRNA 472 5'-GGU-GAA-UGU-CAA-GAC-GCU-GUU-3' (SEQ ID NO: 22) and siRNA 2303 5'-cuc-uuc-cga-ucc-cac-cua-cuu-3' (SEQ ID NO: 23). Negative control siRNA to scrambled GAPDH was from Ambion (Austin, TX).

- Please replace the paragraph on page 69 starting at line 7 with the following text:

Total RNA was extracted using RNA STAT-60 (Tel-Test, Inc. Friendswood TX) from prostate cancer specimens and adjacent normal specimens. For quantitative RT-PCR first strand

cDNA was synthesized from 5 µg of total RNA using SuperScript III (Invitrogen, Carlsbad CA). Quantitative RT-PCR was performed on the Stratagene MX3000P system (Stratagene, La Jolla CA) using SYBR Green I Brilliant Mastermix (Stragene) according to the manufacture's instructions. Optimized reactions for EphB4 and  $\beta$ -actin (used as the normalizer gene) were 150 nM each of the forward primer ( $\beta$ -actin, 5'-GGA-CCT-GAC-TGA-CTA-CCT-A-3' (SEQ ID NO: 24); EphB4, 5'-AAG-GAG-ACC-TTC-ACC-GTC-TT-3' (SEQ ID NO: 25)) and reverse primer ( $\beta$ -actin 5'-TTG-AAG-GTA-GTT-TCG-TGG-AT-3' (SEQ ID NO: 26); EphB4, 5'-TCG-AGT-CAG-GTT-CAC-AGT-CA-3' (SEQ ID NO: 27)) with DNA denaturation/activation of polymerase at 95 °C for 10 min followed by 40 cycles of 95 °C for 30s, 60 °C for 1min, 72 °C for 1min. The specificity of the gene-specific amplification was confirmed by the presence of a single dissociation peak. All reactions were performed in triplicate with RT and no template negative controls.

- Please replace the paragraph on page 75 starting at line 9 with the following text:

Total RNA was reversed transcribed by use of random hexamers (Invitrogen). Primers for EphB4 and EphrinB2 were designed with Primer 3 software. The sequences for all primers are as follows: EPHB4 forward primer and EPHB4 reverse primer (see, e.g., in Example 2); EphrinB2 forward primer and EphrinB2 reverse primer (see, e.g., in Example 6); G3PDH forward primer, 5'-GGAGCCAAAAGGGTCATCAT-3' (SEQ ID NO: 28); G3PDH reverse primer, 5'-GGCATTGCTGCAAAGAAAGAG-3' (SEQ ID NO: 29); Clonetics kit was used for PCR. PCRs were performed with the ABI PCR System 2700 (Applied Biosystem). The PCR conditions were 95 °C for 5 min, followed by 35 cycles of 95 °C for 30 seconds, 60 °C for 30 seconds and 72 °C for 1min.

- Please replace the paragraph on page 75 starting at line 18 with the following text:

Ephrin-B2 and EphB4 PCR products were cloned using the pGEM-T Easy System (Promega, Madison WI) according to the manufacturer's description. The primers and PCR products were 5'-tccgtgtggaagtactgtctg-3' (SEQ ID NO: 30) (forward), 5'-tctggtttggcacagttgag-3' (SEQ ID NO: 31) (reverse), for ephrin-B2 that yielded a 296-bp product and 5'-ctttggaagagaccctgtctg-3' (SEQ ID NO: 32) (forward), 5'-agacgggtgaaggtctccttg-3' (SEQ ID NO: 33), for EphB4 that yielded a 297-bp product. The authenticity and insert orientation were confirmed by DNA sequencing.

- Please replace Table 1 on page 81 starting at line 12 with the following table:

Name	siRNA sequence	<u>SEQ. ID NO:</u>
<b>Eph B4 50:</b>	5' - GAGACCCUGCUGAACACAAUU - 3' 3' - UUCUCUGGGACGACUUGUGUU - 5'	<u>34</u> <u>35</u>
<b>Eph B4 472:</b>	5' - GGUGAAUGUCAAGACGCUGUU - 3' 3' - UCCACUUACAGUUCUGCGAC - 5'	<u>36</u> <u>37</u>
<b>Eph B4 1562:</b>	5' - CAUCACAGCCAGACCCAACUU - 3' 3' - UUGUAGUGUCGGUCUGGGUUG - 5'	<u>38</u> <u>39</u>
<b>Eph B4 2302</b>	5' - CUCUCCGAUCCCACCUACUU - 3' 3' - UUGAGAAGGCUAGGGUGGAUG - 5'	<u>40</u> <u>41</u>

➤ Please replace Table 3 on page 85 starting at line 11 with the following table:

Name	Position	Sequence (5' → 3')	<u>SEQ. ID NO:</u>
Eph B4 AS-1	(552-572)	GTG CAG GGA TAG CAG GGC CAT	<u>42</u>
Eph B4 AS-2	(952-972)	AAG GAG GGG TGG TGC ACG GTG	<u>43</u>
Eph B4 AS-3	(1007-1027)	TTC CAG GTG CAG GGA GGA GCC	<u>44</u>
Eph B4 AS-4	(1263-1285)	GTG GTG ACA TTG ACA GGC TCA	<u>45</u>
Eph B4 AS-5	(1555-1575)	TCT GGC TGT GAT GTT CCT GGC	<u>46</u>
Eph B4 AS-6	(123-140)	GCC GCT CAG TTC CTC CCA	<u>47</u>
Eph B4 AS-7	(316-333)	TGA AGG TCT CCT TGC AGG	<u>48</u>
Eph B4 AS-8	(408-428)	CGC GGC CAC CGT GTC CAC CTT	<u>49</u>
Eph B4 AS-9	(1929-1949)	CTT CAG GGT CTT GAT TGC CAC	<u>50</u>
Eph B4 AS-10	(1980-1999)	ATG GAG GCC TCG CTC AGA AA	<u>51</u>
Eph b4 AS-11	(2138-2158)	CAT GCC CAC GAG CTG GAT GAC	<u>52</u>

➤ Please replace Table 4 bridging pages 92 and 93 with the following table:

Gene	Primer sequence	Product Size (bp)	<u>SEQ. ID NO:</u>
ISH Probe Primers			
ephrin B2	5' - TCC GTG TGG AGT ACT GCT G - 3'	296	<u>53</u>

EphB4	5' -TCT GGT TTG GCA CAG TTG AG-3'	297	<u>54</u>
	5' -CTT TGG AAG AGA CCC TGC TG-3'		<u>55</u>
	5' -AGA CGG TGA AGG TCT CCT TG-3'		<u>56</u>
RT-PCR Primers			
ephrin B2	5' -AGA CAA GAG CCA TGA AGA TC-3'	200	<u>57</u>
	5' -GGA TCC CAC TTC GGA CCC GAG-3'		<u>58</u>
EphB4	5' -TCA GGT CAC TGC ATT GAA CGG G-3'	400	<u>59</u>
	5' -AAC TCG CTC TCA TCC AGT T-3'		<u>60</u>
$\beta$ -actin	5' -GTG GGG CGC CCC AGG CAC CA-3'	546	<u>61</u>
	5' -CTC CTT AAT GTC ACG CAC GAT TTC-3'		<u>62</u>

➤ Please replace Table 5 on page 96 starting at line 9 with the following table:

ephrin B2 264	5' -GCAGACAGAUGCACUAUUAUU-3'	<u>SEQ ID NO: 63</u>
	3' -UUCGUCUGUCUACGUGAUAAU-5'	<u>SEQ ID NO: 64</u>
ephrin B2 63:	5' -CUGCGAUUUCCAAUUCGAUUU-3'	<u>SEQ ID NO: 65</u>
	3' -UUGACGCUAAAGGUUUAGCUA-5'	<u>SEQ ID NO: 66</u>
ephrin B2 137:	5' -GGACUGGUACUAUACCCACUU-3'	<u>SEQ ID NO: 67</u>
	3' -UUCCUGACCAUGAUUGGGUG-5'	<u>SEQ ID NO: 68</u>
Eph B4 50:	5' -GAGACCCUGCUGAACACAAUU-3'	<u>SEQ ID NO: 69</u>
	3' -UUCUCUGGGACGACUUGUGUU-5'	<u>SEQ ID NO: 70</u>
GFP	5' -CGCUGACCCUGAAGUUCAUUU-3'	<u>SEQ ID NO: 71</u>
	3' -UUGCGACUGGGACUUCAGUA-5'	<u>SEQ ID NO: 72</u>

➤ Please replace Table 6 spanning on pages 98-101 with the following table:

Name	Sequence 5'→ 3'	position	Inhibition of EphB4 Expression	Percent reduction in viability	<u>SEQ ID NO:</u>
Eph B4 169	TCA GTA CTG CGG GGC CGG TCC	(2944-2963)	++	36	73
Eph B4 168	TCC TGT CCC ACC CGG GGT TC	(2924-2943)	++	51	74
Eph B4 167	CCG GCT TGG CCT GGG ACT TC	(2904-2923)	+++	66	75
Eph B4 166	ATG TGC TGG ACA CTG GCC AA	(2884-2903)	++++	70	76
Eph B4 165	GAT TTT CTT CTG GTG TCC CG	(2864-2883)	++++	75	77
Eph B4 164	CCA GAG TGA CTC CGA TTC GG	(2844-2863)	++	40	78
Eph B4 163	AGC AGG TCC TCA GCA GAG AT	(2824-2843)	++++	66	79
Eph B4 162	CTG GCT GAC CAG CTC GAA GG	(2804-2823)		25	80
Eph B4 161	AGC CAA AGC CAG CGG CTG CG	(2784-2803)	+	33	81

Eph B4 160	AAA CTT TCT TCG TAT CTT CC	(2763-2783)	+	25	82
Eph B4 159	CAT TTT GAT GGC CCG AAG CC	(2743-2762)	++	40	83
Eph B4 158	ACT CGC CCA CAG AGC CAA AA	(2723-2742)		30	84
Eph B4 157	GCT GAG TAG TGA GGC TGC CG	(2703-2722)	+	25	85
Eph B4 156	CTG GTC CAG GAG AGG GTG TG	(2683-2702)	++	30	86
Eph B4 155	AGG CCC CGC CAT TCT CCC GG	(2663-2682)		25	87
Eph B4 154	GCC ACG ATT TTG AGG CTG GC	(2643-2662)	++	40	88
Eph B4 153	GGG GTT CCG GAT CAT CTT GT	(2623-2642)	++	35	89
Eph B4 152	CCA GGG CGC TGA CCA CCT GG	(2603-2622)	+	30	90
Eph B4 151	GGG AAG CGG GGC CGG GCA TT	(2583-2602)	+	25	91
Eph B4 150	CCG GTC TTT CTG CCA ACA GT	(2563-2582)	++	25	92
Eph B4 149	CCA GCA TGA GCT GGT GGA GG	(2543-2562)	++	20	93
Eph B4 148	GAG GTG GGA CAG TCT GGG GG	(2523-2542)	+	30	94
Eph B4 147	CGG GGG CAG CCG GTA GTC CT	(2503-2522)	++	40	95
Eph B4 146	GTT CAA TGG CAT TGA TCA CG	(2483-2502)	++++	70	96
Eph B4 145	TCC TGA TTG CTC ATG TCC CA	(2463-2482)	++++	80	97
Eph B4 144	GTA CGG CCT CTC CCC AAA TG	(2443-2462)	+++	60	98
Eph B4 143	ACA TCA CCT CCC ACA TCA CA	(2423-2442)	++++	80	99
Eph B4 142	ATC CCG TAA CTC CAG GCA TC	(2403-2422)	++	40	100
Eph B4 141	ACT GGC GGA AGT GAA CTT CC	(2383-2402)	+++	50	101
Eph B4 140	GGA AGG CAA TGG CCT CCG GG	(2363-2382)	++	45	102
Eph B4 139	GCA GTC CAT CGG ATG GGA AT	(2343-2362)	++++	70	103
Eph B4 138	CTT TCC TCC CAG GGA GCT CG	(2323-2342)	++++	70	104
Eph B4 137	TGT AGG TGG GAT CGG AAG AG	(2303-2322)	++	40	105
Eph B4 136	TTC TCC TCC AGG AAT CGG GA	(2283-2302)	++	35	106
Eph B4 135	AAG GCC AAA GTC AGA CAC TT	(2263-2282)	++++	60	107
Eph B4 134	GCA GAC GAG GTT GCT GTT GA	(2243-2262)	++	50	108
Eph B4 133	CTA GGA TGT TGC GAG CAG CC	(2223-2242)	++	40	109
Eph B4 132	AGG TCT CGG TGG ACG TAG CT	(2203-2222)	++	40	110
Eph B4 131	CAT CTC GGC AAG GTA CCG CA	(2183-2202)	+++	50	111
Eph B4 130	TGC CCG AGG CGA TGC CCC GC	(2163-2182)	++	50	112
Eph B4 129	AGC ATG CCC ACG AGC TGG AT	(2143-2162)	++	50	113
Eph B4 128	GAC TGT GAA CTG TCC GTC GT	(2123-2142)	++	50	114
Eph B4 127	TTA GCC GCA GGA AGG AGT CC	(2103-2122)	+++	60	115
Eph B4 126	AGG GCG CCG TTC TCC ATG AA	(2083-2102)	++	50	116
Eph B4 125	CTC TGT GAG AAT CAT GAC GG	(2063-2082)	++++	80	117
Eph B4 124	GCA TGC TGT TGG TGA CCA CG	(2043-2062)	++++	70	118
Eph B4 123	CCC TCC AGG CGG ATG ATA TT	(2023-2042)	++	50	119
Eph B4 122	GGG GTG CTC GAA CTG GCC CA	(2003-2022)	++++	80	120
Eph B4 121	TGA TGG AGG CCT CGC TCA GA	(1983-2002)	++	50	121
Eph B4 120	AAC TCA CGC CGC TGC CGC TC	(1963-1982)	++	40	122
Eph B4 119	CGT GTA GCC ACC CTT CAG GG	(1943-1962)	++++	75	123
Eph B4 118	TCT TGA TTG CCA CAC AGC TC	(1923-1942)	++++	80	124
Eph B4 117	TCC TTC TTC CCT GGG GCC TT	(1903-1922)	++++	70	125
Eph B4 116	GAG CCG CCC CCG GCA CAC CT	(1883-1902)	++	50	126
Eph B4 115	CGC CAA ACT CAC CTG CAC CA	(1863-1882)	++++	60	127
Eph B4 114	ATC ACC TCT TCA ATC TTG AC	(1843-1862)	++++	65	128
Eph B4 113	GTA GGA GAC ATC GAT CTC TT	(1823-1842)	++++	90	129
Eph B4 112	TTG CAA ATT CCC TCA CAG CC	(1803-1822)	++++	70	130
Eph B4 111	TCA TTA GGG TCT TCA TAA GT	(1783-1802)	++++	70	131
Eph B4 110	GAA GGG GTC GAT GTA GAC CT	(1763-1782)	++++	80	132
Eph B4 109	TAG TAC CAT GTC CGA TGA GA	(1743-1762)	++	50	133
Eph B4 108	TAC TGT CCG TGT TTG TCC GA	(1723-1742)	++	45	134
Eph B4 107	ATA TTC TGC TTC TCT CCC AT	(1703-1722)	++++	70	135
Eph B4 106	TGC TCT GCT TCC TGA GGC AG	(1683-1702)	++++	70	136

Eph B4 105	AGA ACT GCG ACC ACA ATG AC	(1663-1682)	++	40	137
Eph B4 104	CAC CAG GAC CAG GAC CAC AC	(1643-1662)	++++	70	138
Eph B4 103	CCA CGA CTG CCG TGC CCG CA	(1623-1642)	++	40	139
Eph B4 102	ATC AGG GCC AGC TGC TCC CG	(1603-1622)	+++	50	140
Eph B4 101	CCA GCC CTC GCT CTC ATC CA	(1583-1602)	++++	80	141
Eph B4 100	GTT GGG TCT GGC TGT GAT GT	(1563-1582)	++++	80	142
Eph B4 99	TCC TGG CCG AAG GGC CCG TA	(1543-1562)	++	35	143
Eph B4 98	GCC GGC CTC AGA GCG CGC CC	(1523-1542)	++	50	144
Eph B4 97	GTA CCT GCA CCA GGT AGC TG	(1503-1522)	++++	80	145
Eph B4 96	GCT CCC CGC TTC AGC CCC CG	(1483-1502)	++	50	146
Eph B4 95	CAG CTC TGC CCG GTT TTC TG	(1463-1482)	++	50	147
Eph B4 94	ACG TCT TCA GGA ACC GCA CG	(1443-1462)	++++	80	148
Eph B4 93	CTG CTG GGA CCC TCG GCG CC	(1423-1442)	++	40	149
Eph B4 92	CTT CTC ATG GTA TTT GAC CT	(1403-1422)	++++	80	150
Eph B4 91	CGT AGT CCA GCA CAG CCC CA	(1383-1402)	++++	85	151
Eph B4 90	CTG GGT GCC CGG GGA ACA GC	(1363-1382)	+++	50	152
Eph B4 89	CCA GGC CAG GCT CAA GCT GC	(1343-1462)	++++	70	153
Eph B4 88	TGG GTG AGG ACC GCG TCA CC	(1323-1342)	++	40	154
Eph B4 87	CGG ATG TCA GAC ACT GCA GG	(1303-1322)	++++	60	155
Eph B4 86	AGG TAC CTC TCG GTC AGT GG	(1283-1302)	++	50	156
Eph B4 85	TGA CAT TGA CAG GCT CAA AT	(1263-1282)	++++	80	157
Eph B4 84	GGG ACG GGC CCC GTG GCT AA	(1243-1262)	++	50	158
Eph B4 83	GGA GGA TAC CCC GTT CAA TG	(1223-1242)	+++	60	159
Eph B4 82	CAG TGA CCT CAA AGG TAT AG	(1203-1222)	++++	70	160
Eph B4 81	GTG AAG TCA GGA CGT AGC CC	(1183-1202)	+++	60	161
Eph B4 80	TCG AAC CAC CAC CCA GGG CT	(1163-1182)	+++	50	162
Eph B4 79	CCA CCA GGT CCC GGG GGC CG	(1143-1162)	++	40	163
Eph B4 78	GGG TCA AAA GTC AGG TCT CC	(1123-1142)	++++	70	164
Eph B4 77	CCC GCA GGG CGC ACA GGA GC	(1103-1122)	+++	60	165
Eph B4 76	CTC CGG GTC GGC ACT CCC GG	(1083-1102)	+++	60	166
Eph B4 75	CAG CGG AGG GCG TAG GTG AG	(1063-1082)	++	40	167
Eph B4 74	GTC CTC TCG GCC ACC AGA CT	(1043-1062)	++	50	168
Eph B4 73	CCA GGG GGG CAC TCC ATT CC	(1023-1042)	++	50	169
Eph B4 72	AGG TGC AGG GAG GAG CCG TT	(1003-1022)	++++	70	170
Eph B4 71	CAG GCG GGA AAC CAC GCT CC	(983-1002)	++	40	171
Eph B4 70	GCG GAG CCG AAG GAG GGG TG	(963-982)	+++	50	172
Eph B4 69	GTG CAG GGT GCA CCC CGG GG	(943-962)	+++	50	173
Eph B4 68	GTC TGT GCG TGC CCG GAA GT	(923-942)	++	40	174
Eph B4 67	ACC CGA GCG GGC ACT GGC AG	(903-922)	++	40	175
Eph B4 66	ACG GCT GAT CCA ATG GTG TT	(883-902)	++	50	176
Eph B4 65	AGA GTG GCT ATT GGC TGG GC	(863-882)	++++	60	177
Eph B4 64	ATG GCT GGC AGG ACC CTT CT	(843-862)	++++	80	178
Eph B4 63	CCT GAC AGG GGC TTG AAG GT	(823-842)	++++	80	179
Eph B4 62	GCC CTG GGC ACA GGC TCG GC	(803-822)	+++	70	180
Eph B4 61	ACT TGG TGT TCC CCT CAG CT	(783-802)	++++	80	181
Eph B4 60	GCC TCG AAC CCC GGA GCA CA	(763-782)	+++	50	182
Eph B4 59	GCT GCA GCC CGT GAC CGG CT	(743-762)	+++	50	183
Eph B4 58	GTT CGG CCC ACT GGC CAT CC	(723-742)	++	45	184
Eph B4 57	TCA CGG CAG TAG AGG CTG GG	(703-722)	+++	70	185
Eph B4 56	GCT GGG GCC AGG GGC GGG GA	(683-702)	++	50	186
Eph B4 55	CGG CAT CCA CCA CGC AGC TA	(663-682)	++	50	187
Eph B4 54	CCG GCC ACG GGC ACA ACC AG	(643-662)	++	50	188
Eph B4 53	CTC CCG AGG CAC AGT CTC CG	(623-642)	+++	50	189
Eph B4 52	GGA ATC GAG TCA GGT TCA CA	(603-622)	++++	90	190
Eph B4 51	GTC AGC TGG GCG CAC TTT TT	(583-602)	+++	70	191



Eph B4 50	GTA GAA GAG GTG CAG GGA TA	(563-582)	++++	80	192
Eph B4 49	GCA GGG CCA TGC AGG CAC CC	(543-562)	++++	80	193
Eph B4 48	TGG TCC TGG AAG GCC AGG TA	(523-542)	++++	90	194
Eph B4 47	GAA GCC AGC CTT GCT GAG CG	(503-522)	++++	80	195
Eph B4 46	GTC CCA GAC GCA GCG TCT TG	(483-502)	++	40	196
Eph B4 45	ACA TTC ACC TTC CCG GTG GC	(463-482)	+++	50	197
Eph B4 44	CTC GGC CCC AGG GCG CTT CC	(443-462)	++	50	198
Eph B4 43	GGG TGA GAT GCT CCG CGG CC	(423-442)	+++	60	199
Eph B4 42	ACC GTG TCC ACC TTG ATG TA	(403-422)	++++	80	200
Eph B4 41	GGG GTT CTC CAT CCA GGC TG	(383-402)	++++	80	201
Eph B4 40	GCG TGA GGG CCG TGG CCG TG	(363-382)	++	50	202
Eph B4 39	TCC GCA TCG CTC TCA TAG TA	(343-362)	+++	60	203
Eph B4 38	GAA GAC GGT GAA GGT CTC CT	(323-342)	++++	80	204
Eph B4 37	TGC AGG AGC GCC CAG CCC GA	(303-322)	+++	50	205
Eph B4 36	GGC AGG GAC AGG CAC TCG AG	(283-302)	+++	45	206
Eph B4 35	CAT GGT GAA GCG CAG CGT GG	(263-282)	++	50	207
Eph B4 34	CGT ACA CGT GGA CGG CGC CC	(243-262)	++	40	208
Eph B4 33	CGC CGT GGG ACC CAA CCT GT	(223-242)	+++	60	209
Eph B4 32	GCG AAG CCA GTG GGC CTG GC	(203-222)	++++	70	210
Eph B4 31	CCG GGG CAC GCT GCA CGT CA	(183-202)	+++	60	211
Eph B4 30	CAC ACT TCG TAG GTG CGC AC	(163-182)	+++	70	212
Eph B4 29	GCT GTG CTG TTC CTC ATC CA	(143-162)	++++	80	213
Eph B4 28	GGC CGC TCA GTT CCT CCC AC	(123-142)	++	40	214
Eph B4 27	TGC CCG TCC ACC TGA GGG AA	(103-122)	++	50	215
Eph B4 26	TGT CAC CCA CTT CAG ATC AG	(83-102)	++++	70	216
Eph B4 25	CAG TTT CCA ATT TTG TGT TC	(63-82)	++++	70	217
Eph B4 24	AGC AGG GTC TCT TCC AAA GC	(43-62)	++++	80	218
Eph B4 23	TGC GGC CAA CGA AGC CCA GC	(23-42)	++	50	219
Eph B4 22	AGA GCA GCA CCC GGA GCT CC	(3-22)	+++	50	220
Eph B4 21	AGC AGC ACC CGG AGC TCC AT	(1-20)	+++	50	221
Additional antisense probes described in the specification					
EphB4 AS-1	GTG CAG GGA TAG CAG GGC CAT	(552-572)			222
EphB4 AS-2	AAG GAG GGG TGG TGC ACG GTG	(952-972)			223
EphB4 AS-3	TTC CAG GTG CAG GGA GGA GCC	(1007-1027)			224
EphB4 AS-4	GTG GTG ACA TTG ACA GGC TCA	(1263-1285)			225
EphB4 AS-5	TCT GGC TGT GAT GTT CCT GGC	(1555-1575)			226
EphB4 AS-6	GCC GCT CAG TTC CTC CCA	(123-140)			227
EphB4 AS-7	TGA AGG TCT CCT TGC AGG	(316-333)			228
EphB4 AS-8	CGC GGC CAC CGT GTC CAC CTT	(408-428)			229
EphB4 AS-9	CTT CAG GGT CTT GAT TGC CAC	(1929-1949)			230
EphB4 AS-10	ATG GAG GCC TCG CTC AGA AA	(1980-1999)			231
EphB4 AS-11	CAT GCC CAC GAG CTG GAT GAC	(2138-2158)			232

➤ Please replace Table 7 spanning on pages 101-103 with the following table:

RNAi	EphB4 RNAi sequence	Inhibition of EphB4 Expression	Percent reduction in viability	SEQ ID NO:
1	446 aaattggaaactgctgatctg 466			233

2	447	aattggaaactgctgatctga	467	+++	70	<u>234</u>
3	453	aaactgctgatctgaagtggg	473	++++	70	<u>235</u>
4	454	aactgctgatctgaagtgggt	474	+++	80	<u>236</u>
5	854	aatgtcaagacgctgcgtctg	874	+++	65	<u>237</u>
6	467	aagtgggtgacattccctcag	487	+	35	<u>238</u>
7	848	aaggtgaatgtcaagacgctg	868	++	50	<u>239</u>
8	698	aaggagaccttcaccgtcttc	718	+++	75	<u>240</u>
9	959	aaaaagtgcgccagctgact	979	+	40	<u>241</u>
10	1247	aatagccactctaaccatt	1267	++	50	<u>242</u>
11	1259	aacaccattggatcagccgtc	1279	++	50	<u>243</u>
12	1652	aatgtcaccactgaccgagag	1672	+	35	<u>244</u>
13	1784	aaataccatgagaagggcgcc	1804	+++	65	<u>245</u>
14	1832	aagacgtcagaaaaccgggca	1852	+	30	<u>246</u>
15	1938	aacatcacagccagaccaac	19	++	50	<u>247</u>
16	2069	aagcagagcaatgggagagaa	2089	++++	75	<u>248</u>
17	2078	aatgggagagaagcagaatat	2098	+++	65	<u>249</u>
18	2088	aagcagaatatcggacaaac	2108	+++	70	<u>250</u>
19	2094	aatattcggacaaacacggac	2114	++	40	<u>251</u>
20	2105	aaacacggacagtatctcatc	2125	++	50	<u>252</u>
21	2106	aacacggacagtatctcatcg	2126	+	35	<u>253</u>
22	2197	aaaagagatcgatgtctccta	2217	+++	65	<u>254</u>
23	2174	aatgaggctgtgagggaaattt	2194	++	50	<u>255</u>
24	2166	aagaccctaagtggctgtga	2186	++	50	<u>256</u>
25	2198	aaagagatcgatgtctcctac	2218	+++	55	<u>257</u>
26	2199	aagagatcgatgtctcctacg	2219	+++	70	<u>258</u>
27	2229	aagaggtgattggtgcaggtg	2249	+	33	<u>259</u>
28	2222	aagattgaagaggtgattggt	2242	+	30	<u>260</u>
29	2429	aacagcatgcccgatgatt	2449	++	40	<u>261</u>
30	2291	aagaaggagagctgtgtggca	2311	+++	50	<u>262</u>
31	2294	aaggagagctgtgtggcaatc	2314	+++	60	<u>263</u>
32	2311	aatcaagaccctgaagggagg	2331	+++	70	<u>264</u>
33	2497	aaacgacggacagttcacagt	2517	+	35	<u>265</u>
34	2498	aacgacggacagttcacagtc	2518	+	40	<u>266</u>
35	2609	aacatcctagtcaacagcaac	2629	++	50	<u>267</u>
36	2621	aacagcaacctcgtctgcaaa	2641	+	35	<u>268</u>
37	2678	aactcttccgatcccacctac	2698	++	50	<u>269</u>
38	2640	aagtgtctgactttggccttt	2660	+++	70	<u>270</u>
39	2627	aacctcgtctgcaaaagtgtct	2647	++	50	<u>271</u>
40	2639	aaagtgtctgactttggcctt	2659	+	25	<u>272</u>
41	2852	aatcaggacgtgatcaatgcc	2872	+++	75	<u>273</u>

42	2716	aaagattcccatccgatggac	2736	++	50	<u>274</u>
43	2717	aagattcccatccgatggact	2737	++	60	<u>275</u>
44	2762	aagttcacttccgccagtgat	2782	+++	70	<u>276</u>
45	3142	aagatacgaagaaagtttcgc	3162	++	50	<u>277</u>
46	3136	aatgggaagatacgaagaaag	3156	+++	66	<u>278</u>
47	2867	aatgccattgaacaggactac	2887			<u>279</u>
48	3029	aaaatcgtggcccgaggagaat	3049	+	33	<u>280</u>
49	3254	aaaatcttggccagtgtccag	3274	++	50	<u>281</u>
50	3255	aaatcttggccagtgtccagc	3275	+++	75	<u>282</u>
51	3150	aagaaagtttcgcagccgctg	3170	+++	80	<u>283</u>
52	3251	aagaaaatcttggccagtgtc	3271	++	50	<u>284</u>
53	3256	aatcttggccagtgtccagca	3276	++	50	<u>285</u>
Additional RNai probes described in specification						
Eph B4 50	gagaccugcugaacacaaau					<u>286</u>
Eph B4 472	ggugaaugucaagacgcuguu					<u>287</u>
Eph B4 1562	caucacagccagacccaacuu					<u>288</u>
siRNA 2303	cucuuccgaucccaccuacuu					<u>289</u>
Eph B4 2302	cucuuccgaucccaccuacuu					<u>290</u>

➤ Please replace Table 8 bridging pages 103 and 104 with the following table:

	sequence	Coding region	Percent reduction in viability	Inhibition of Ephrin B2 Expression	SEQ ID NO:
Ephrin AS-51	TCA GAC CTT GTA GTA AAT GT	(983-1002)	35	++	<u>291</u>
Ephrin AS-50	TCG CCG GGC TCT GCG GGG GC	(963-982)	50	+++	<u>292</u>
Ephrin AS-49	ATC TCC TGG ACG ATG TAC AC	(943-962)	45	++	<u>293</u>
Ephrin AS-48	CGG GTG CCC GTA GTC CCC GC	(923-942)	35	++	<u>294</u>
Ephrin AS-47	TGA CCT TCT CGT AGT GAG GG	(903-922)	40	+++	<u>295</u>
Ephrin AS-46	CAG AAG ACG CTG TCC GCA GT	(883-902)	40	++	<u>296</u>
Ephrin AS-45	CCT TAG CGG GAT GAT AAT GT	(863-882)	35	++	<u>297</u>
Ephrin AS-44	CAC TGG GCT CTG AGC CGT TG	(843-862)	60	+++	<u>298</u>
Ephrin AS-43	TTG TTG CCG CTG CGC TTG GG	(823-842)	40	++	<u>299</u>
Ephrin AS-42	TGT GGC CAG TGT GCT GAG CG	(803-822)	40	++	<u>300</u>
Ephrin AS-41	ACA GCG TGG TCG TGT GCT GC	(783-802)	70	+++	<u>301</u>

Ephrin AS-40	GGC GAG TGC TTC CTG TGT CT	(763-782)	80	++++	<u>302</u>
Ephrin AS-39	CCT CCG GTA CTT CAG CAA GA	(743-762)	50	+++	<u>303</u>
Ephrin AS-38	GGA CCA CCA GCG TGA TGA TG	(723-742)	60	+++	<u>304</u>
Ephrin AS-37	ATG ACG ATG AAG ATG ATG CA	(703-722)	70	+++	<u>305</u>
Ephrin AS-36	TCC TGA AGC AAT CCC TGC AA	(683-702)	60	+++	<u>306</u>
Ephrin AS-35	ATA AGG CCA CTT CGG AAC CG	(663-682)	45	++	<u>307</u>
Ephrin AS-34	AGG ATG TTG TTC CCC GAA TG	(643-662)	50	+++	<u>308</u>
Ephrin AS-33	TCC GGC GCT GTT GCC GTC TG	(623-642)	75	+++	<u>309</u>
Ephrin AS-32	TGC TAG AAC CTG GAT TTG GT	(603-622)	60	+++	<u>310</u>
Ephrin AS-31	TTT ACA AAG GGA CTT GTT GT	(583-602)	66	+++	<u>311</u>
Ephrin AS-30	CGA ACT TCT TCC ATT TGT AC	(563-582)	50	++	<u>312</u>
Ephrin AS-29	CAG CTT CTA GTT CTG GAC GT	(543-562)	50	+++	<u>313</u>
Ephrin AS-28	CTT GTT GGA TCT TTA TTC CT	(523-542)	70	+++	<u>314</u>
Ephrin AS-27	GGT TGA TCC AGC AGA ACT TG	(503-522)	65	+++	<u>315</u>
Ephrin AS-26	CAT CTT GTC CAA CTT TCA TG	(483-502)	75	+++	<u>316</u>
Ephrin AS-25	AGG ATC TTC ATG GCT CTT GT	(463-482)	60	+++	<u>317</u>
Ephrin AS-24	CTG GCA CAC CCC TCC CTC CT	(443-462)	45	++	<u>318</u>
Ephrin AS-23	GGT TAT CCA GGC CCT CCA AA	(423-442)	50	+++	<u>319</u>
Ephrin AS-22	GAC CCA TTT GAT GTA GAT AT	(403-422)	50	+++	<u>320</u>
Ephrin AS-21	AAT GTA ATA ATC TTT GTT CT	(383-402)	60	+++	<u>321</u>
Ephrin AS-20	TCT GAA ATT CTA GAC CCC AG	(363-382)	60	+++	<u>322</u>
Ephrin AS-19	AGG TTA GGG CTG AAT TCT TG	(343-362)	75	+++	<u>323</u>
Ephrin AS-18	AAA CTT GAT GGT GAA TTT GA	(323-342)	60	+++	<u>324</u>
Ephrin AS-17	TAT CTT GGT CTG GTT TGG CA	(303-322)	50	++	<u>325</u>
Ephrin AS-16	CAG TTG AGG AGA GGG GTA TT	(283-302)	40	++	<u>326</u>
Ephrin AS-15	TTC CTT CTT AAT AGT GCA TC	(263-282)	66	+++	<u>327</u>
Ephrin AS-14	TGT CTG CTT GGT CTT TAT CA	(243-262)	70	++++	<u>328</u>
Ephrin AS-13	ACC ATA TAA ACT TTA TAA TA	(223-242)	50	+++	<u>329</u>
Ephrin AS-12	TTC ATA CTG GCC AAC AGT TT	(203-222)	50	+++	<u>330</u>
Ephrin AS-11	TAG AGT CCA CTT TGG GGC AA	(183-202)	70	++++	<u>331</u>
Ephrin AS-10	ATA ATA TCC AAT TTG TCT CC	(163-182)	70	++++	<u>332</u>

Ephrin AS-9	TAT CTG TGG GTA TAG TAC CA	(143-162)	80	++++	<u>333</u>
Ephrin AS-8	GTC CTT GTC CAG GTA GAA AT	(123-142)	60	+++	<u>334</u>
Ephrin AS-7	TTG GAG TTC GAG GAA TTC CA	(103-122)	80	++++	<u>335</u>
Ephrin AS-6	ATA GAT AGG CTC TAA AAC TA	(83-102)	70	+++	<u>336</u>
Ephrin AS-5	TCG ATT TGG AAA TCG CAG TT	(63-82)	50	+++	<u>337</u>
Ephrin AS-4	CTG CAT AAA ACC ATC AAA AC	(43-62)	80	++++	<u>338</u>
Ephrin AS-3	ACC CCA GCA GTA CTT CCA CA	(23-42)	85	++++	<u>339</u>
Ephrin AS-2	CGG AGT CCC TTC TCA CAG CC	(3-22)	70	+++	<u>340</u>
Ephrin AS-1	GAG TCC CTT CTC ACA GCC AT	(1-20)	80	++++	<u>341</u>

➤ Please replace Table 9 spanning on pages 101-103 with the following table:

RNAi Sequence and homology with other human genes.			Percent reduction in viability	Inhibition of Ephrin B2 Expression	RNAi no.	SEQ ID NO:
89	aactgcgatttccaaatcgat	109	80	++++	1	<u>342</u>
141	aactccaaatttctacctgga	161	70	++++	2	<u>343</u>
148	aatttctacctggacaaggac	168	75	+++	3	<u>344</u>
147	aaatttctacctggacaagga	167	60	+++	4	<u>345</u>
163	aaggactggtactatacccac	183	40	++	5	<u>346</u>
217	aagtggactctaaaactggtg	237	80	++++	6	<u>347</u>
229	aaactgttggccagtatgaat	249	50	+++	7	<u>348</u>
228	aaaactgttggccagtatgaa	248	80	++++	8	<u>349</u>
274	aagaccaagcagacagatgca	294	80	++++	11	<u>350</u>
273	aaagaccaagcagacagatgc	293	60	+++	12	<u>351</u>
363	aagtttcaagaattcagccct	383	66	+++	13	<u>352</u>
370	agaattcagccctaacctct	390	50	+++	14	<u>353</u>
373	aattcagccctaacctctggg	393	50	+++	15	<u>354</u>
324	aactgtgccaaccagaccaa	344	90	++++	16	<u>355</u>
440	aatgggtctttggagggcct	460	80	++++	17	<u>356</u>
501	aagatcctcatgaaagtggga	521	50	+++	18	<u>357</u>
513	aaagttggacaagatgcaagt	533	50	+++	19	<u>358</u>
491	aagagcatgaagatcctcat	511	50	+++	20	<u>359</u>
514	aagttggacaagatgcaagtt	534	66	+++	21	<u>360</u>
523	aagatgcaagttctgctggat	543	66	+++	22	<u>361</u>
530	aagttctgctggatcaaccag	550	50	+++	23	<u>362</u>

545	aaccaggaataaagatccaac	565	35	++	24	<u>363</u>
555	aaagatccaacaagacgtcca	575	40	++	25	<u>364</u>
556	aagatccaacaagacgtccag	576	60	+++	26	<u>365</u>
563	aacaagacgtccagaactaga	583	60	+++	27	<u>366</u>
566	aagacgtccagaactagaagc	586	70	+++	28	<u>367</u>
593	aaatggaagaagttcgacaac	613	75	++++	29	<u>368</u>
577	aactagaagctggtacaaatg	597	66	+++	30	<u>369</u>
594	aatggaagaagttcgacaaca	614	35	++	31	<u>370</u>
583	aagctggtacaaatggaagaa	603	50	+++	32	<u>371</u>
611	aacaagtccctttgtaaaacc	631	70	++++	33	<u>372</u>
599	aagaagttcgacaacaagtcc	619	70	++++	34	<u>373</u>
602	aagttcgacaacaagtcctt	622	80	++++	35	<u>374</u>
626	aaaaccaaattccaggttctag	646	50	+++	36	<u>375</u>
627	aaaccaaattccaggttctagc	647	25	+	37	<u>376</u>
628	aaccaaattccaggttctagca	648	30	++	38	<u>377</u>
632	aatccaggttctagcacaga	652	60	+++	39	<u>378</u>
633	aatccaggttctagcacagac	653	40	++	40	<u>379</u>
678	aacaacatcctcggttccgaa	698	30	++	41	<u>380</u>
681	aacatcctcggttccgaagtg	701	20	+	42	<u>381</u>
697	aagtggccttatttgcaggga	717	30	++	43	<u>382</u>
Additional Ephrin B2 RNAi probes described in the specifications						
GCAGACAGAUGCACUAUUAUU					ephrin B2 264	<u>383</u>
CUGCGAUUUCCAAUCGAUUU					ephrin B2 63	<u>384</u>
GGACUGGUACUAUACCCACUU					ephrin B2 137	<u>385</u>